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A CONVENIENT ACCESS TO 1,5-ANHYDROKETOSES[1)]

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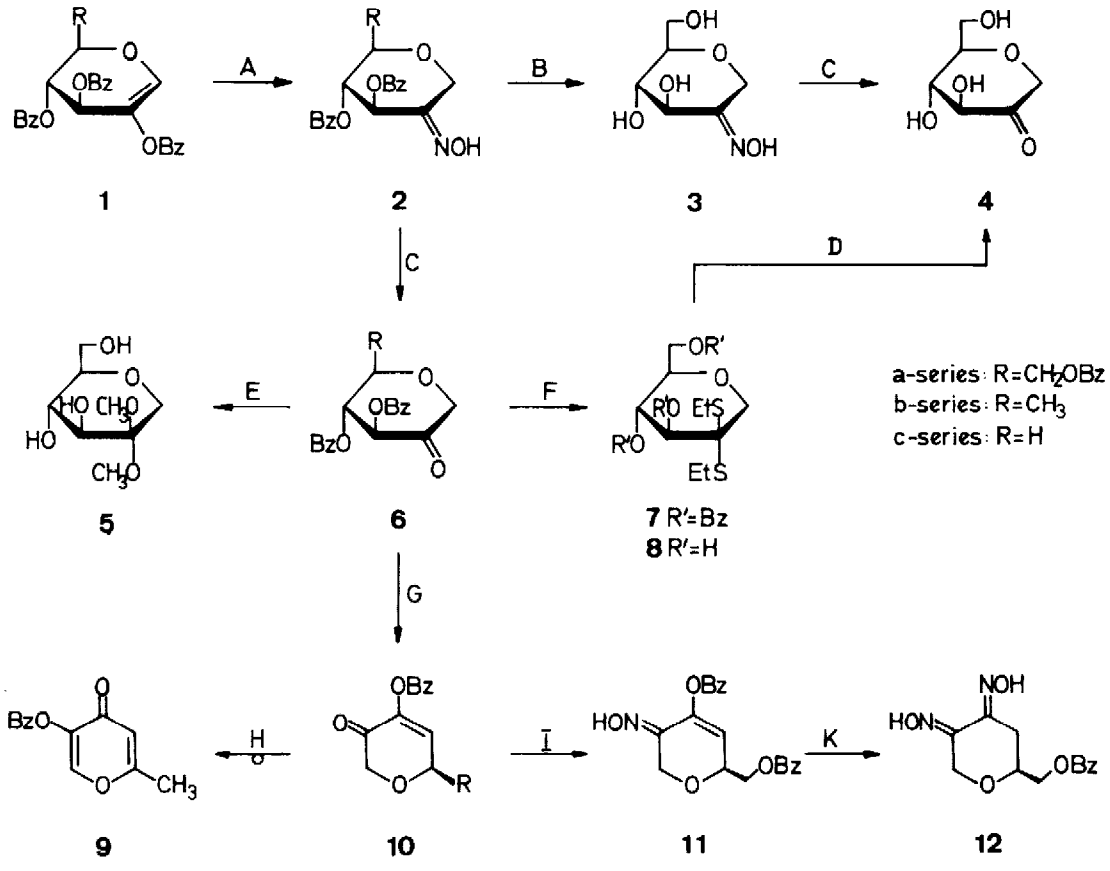
A convenient, versatile entry into the 1,5-anhyroketose series is described and their conversion into enolones, enolone oximes and γ-pyrones.

Despite the ready availability of 2-hydroxyglycal esters *1*[2)], which de facto are derivatives of the enol form of 1,5-anhydroketoses, none of the free 1,5-anhydroketoses are known[3)]. Previous attempts at base-catalyzed deacylation have consistently been unsuccessful, leading to amorphous, reducing products with incorrect analytical data[4)] — a failure that is obviously due to the liberation of the 2-keto function and subsequent 3,4-elimination of carboxylic acid prior to further deacylation[5)]. We now report on a ready access to 1,5-anhydroketoses from their peracylated oximes now available from 2-hydroxyglycal esters by hydroxylaminolysis[1)], as well as on their conversion into enolones and enolone oximes.

The benzoylated ketoximes *2* are crystalline, stable intermediates, which survive a variety of conditions, as e.g. those of alkylation (methyl iodide/silver oxide), acylation (benzoyl chloride/pyridine) and sulfonylation (tosyl chloride/pyridine), affording the respective N-*O*-substituted derivatives[7)]. On exposure to Zemplen conditions (B in Scheme 1), a clean de-*O*-benzoylation is effected to afford e.g. the highly crystalline 1,5-anhydro-D-fructose oxime (*3*) from its tribenzoate (*2a*). In contrast, benzoylated 1,5-anhydroketoses *6* obtained in high yields on deoximation of the ketoximes *2* with acetaldehyde/HCl in acetonitrile[8)] (cf. Table 1), give complex mixtures on deacylation under Zemplen conditions, obviously due to elimination to enolones of type *10* and subsequent aldol condensations and/or benzilic acid rearrangements of the 2,3-diuloses formed. Thus, the oximes are an effective means for carbonyl protection in that such base-catalyzed β-eliminations are prevented.

Acid-catalyzed reactions, e.g. ketalizations, are readily feasible with the *O*-benzoylated ketoses *6*; treatment with trimethoxymethane/HCl or ethanethiol/BF_3 affords the respective *O*- and *S*-acetals, which are easily deacylated (*6a* → *5* and *6a* → *7* → *8*, cf. Table). Preparation of the free 1,5-anhydroketoses, such as *4*, can be effected equally by demercaptalization of the diethyl dithioacetal *8* with mercuric chloride/cadmium carbonate or by deoximation of the oxime *3*. Both routes afforded *4* as an amorphous, chromatographically homogeneous product. The apparent equilibrium between monomeric and dimeric forms of *4* is presently being studied. The ketose was characterized by reduction with sodium borohydride to give a mixture of the D-*gluco* and D-*manno*-1,5-anhydrohexitols.



Scheme 1. Reaction conditions: *A*, $NH_2OH \cdot HCl$/pyridine, 4 d, 25°C; *B*, 0,1 N methanolic sodium methoxide, 1 h, 5°C; *C*, Acetaldehyde/hydrochloric acid in acetonitrile, 5 - 8 h, 25°C; *D*, $HgCl_2/CdCO_3$ in water, 25°C; *E*, Trimethoxymethane/methanol/1% HCl, 3 d at 40°C followed by sodium methoxide/methanol treatment; *F*, EtSH/BF_3-etherate in $CHCl_3$, 1 h, 25°C; *G*, Pyridine/benzene (1:10), 1 h, 60°C; *H*, K_2CO_3 in moist DMSO, 12 h, 25°C; *I*, $NH_2OH \cdot HCl$ in ethanol/pyridine (50:1), 1 h, 25°C; *K*, $NH_2OH \cdot HCl$/sodium acetate in ethanol, 12 h, 25°C.

As expected from the high propensity of peracylated pyranosuloses for elimination of an acyloxy group in β-position to the carbonyl function[9], the *O*-benzoyl-ketoses *6* readily form the enolone system *10* by loss of benzoic acid, brief treatment with pyridine in benzene being sufficient for the conversion. The integrity at the remaining chiral center is retained on oximation which can be conducted to yield either the enolone oxime *11* or, by hydroxylaminolysis of the enolic ester function, the respective dioxime *12* (cf. Table). On treatment with potassium carbonate in aqueous DMSO, however, *10a* is expectedly[10] converted into *O*-benzoyl-allomaltol (*9*) via 5,6-elimination of benzoic acid, protonation of the exocyclic double bond and benzoyl group migration.

Table 1. Conditions of preparation, yield and physical data

Compd.[a]	Yield [%] (educt[b], cond.[c])	m.p. [°C]	$[\alpha]_D$	(°C, c, solvent)
2b	68 (*1b*, A)	159-160	-123	(21, 0.2, $CHCl_3$)
3	65 (*2a*, B)	178-180	-43	(21, 0.3, H_2O)
4	73 (*8*, D), 60 (*3*, C)	amorph	-13	(22, 0.5, H_2O)
5	36 (*6a*, E)	134-135	+29	(24, 1, CH_3OH)
6a	88 (*2a*, C)	126-127	-24	(20, 0.8, $CHCl_3$)
6b	73 (*2b*, C)	123-124	-110	(21, 1.1, $CHCl_3$)
6c	65 (*2c*, C)	92- 93	-103	(21, 0.6, $CHCl_3$)
7	85 (*6a*, F)	syrup	-49	(23, 1, $CHCl_3$)
8	91 (*7*, B)	92- 94	-51	(24, 1, CH_3OH)
10a	74 (*6a*, G)	104-105	-16	(22, 1, $CHCl_3$)
10b	87 (*6b*, G)	109-110	+9.4	(21, 0.3, $CHCl_3$)
10c	82 (*6c*, G)	111-112	---	---
11	67 (*10a*, I)	133-134	-22	(21, 0.1, $CHCl_3$)
12	79 (*11*, K)	187-189	-111	(21, 0.5, C_5H_5N)

a) Values for combustion analysis, molecular weights (FD-MS spectra) and ^{1}H-NMR data are in accord with the structures and configurations assigned. — b) Educt *1b*: E. Fischer and F.W. Lichtenthaler, *Angew. Chem. Int. Ed. Engl.* 13, 546 (1974); G. Ekborg, P.J. Garegg and S. Josephson, *Carbohydr. Res.* 65, 301 (1978). — Educts *2a*, *2b* and *2c*: ref. 1. — c) Conditions A - K, cf. scheme 1.

This approach to 1,5-anhydro-D-fructose and its simple derivatives sets a promising basis for the projected syntheses of other 1,5-anhydroketoses, e.g. of *tagato*- and *psico*-configuration, as well as those derived from disaccharides, on which we hope to report at a later date.

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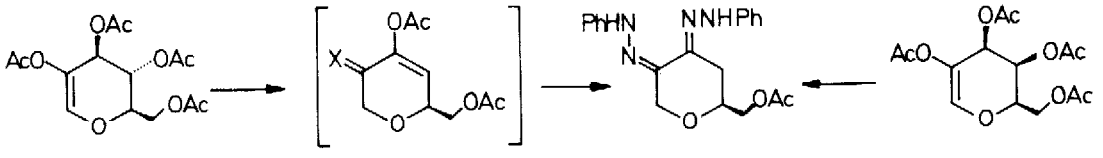
5) The high propensity towards 3,4-elimination of carboxylic acid is similarly shown by the conversion of tetra-O-acetyl-1,5-anhydro-D-*arabino*-hex-1-enitol (i) or its D-*lyxo* analog (iv) into osazone (iii) on heating with phenylhydrazine[6], conceivably *via* an enolone intermediate of type (ii, X = O) or its phenylhydrazone (X = NNHPh).



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